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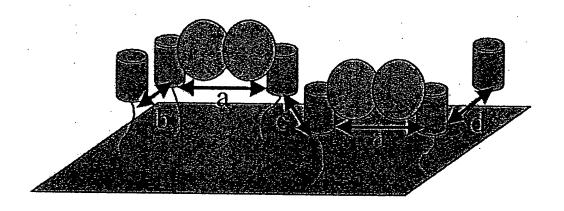
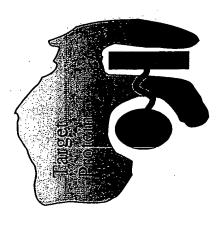


FIG. 1

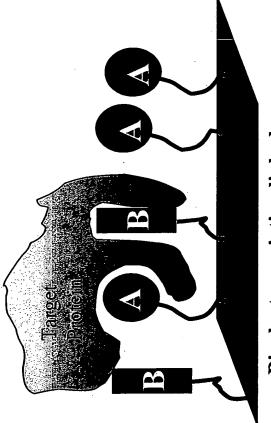


Fesik, Ellman, others



High affinity bivalent ligand

Two low affinity monovalent ligands

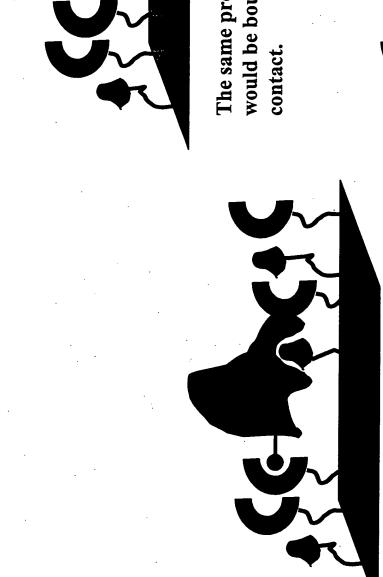


Bivalent association linked by the surface

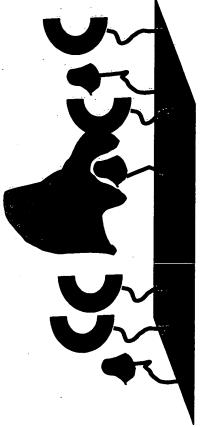
FIG. 3

FIG. 4

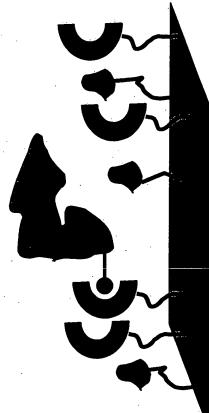




High affinity binding of a particular post-translationally modified protein through a two-point contact.

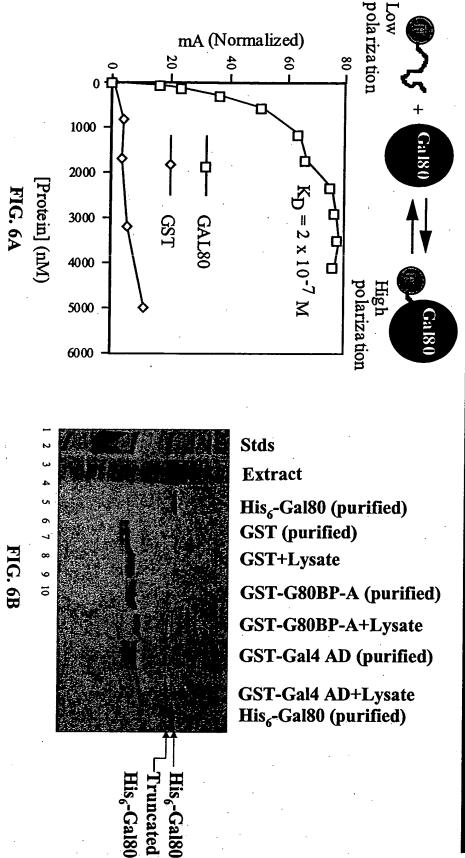


The same protein lacking the modification would be bound weakly via a one-point

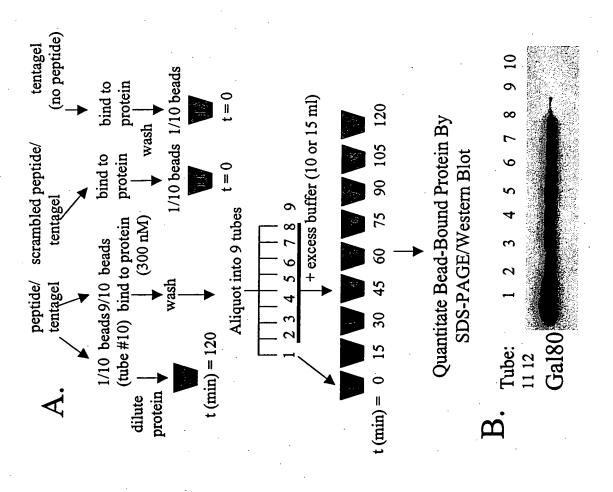


Other proteins containing the same modification would be bound weakly via a one-point contact

G80BP-B: NEDWERDDQNPWDKLWMNRA G80BP-A: YDQDMQNNTFDDLFWKEGHR GAL4 AD: MDQTAYNAFGITTGMFNTTTMDDVYNYLFDDEDT







A. [His6Gal80] (nM): 8 4 2 1.5 1 0.75 0.4 0.3 0.2 His6Gal80 (ng): 200 100 50 37.5 25 17.5 10 7.5 5



FIG. 8

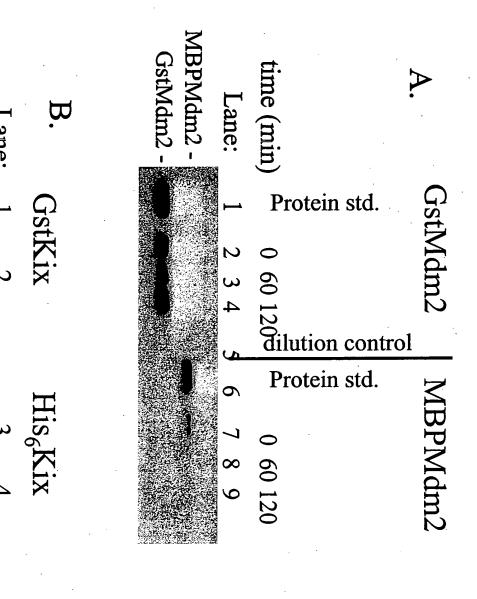


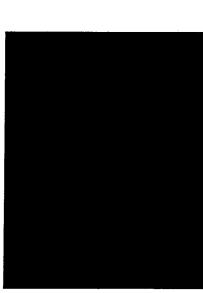
FIG. 9

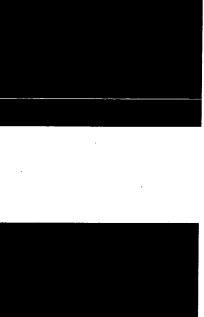


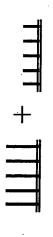
Peptides: VFFKDKKF LLLL MPR

MBP-mdm2 fusion
MPRMDYWEDL

MECA |







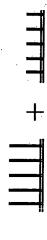


FIG. 10

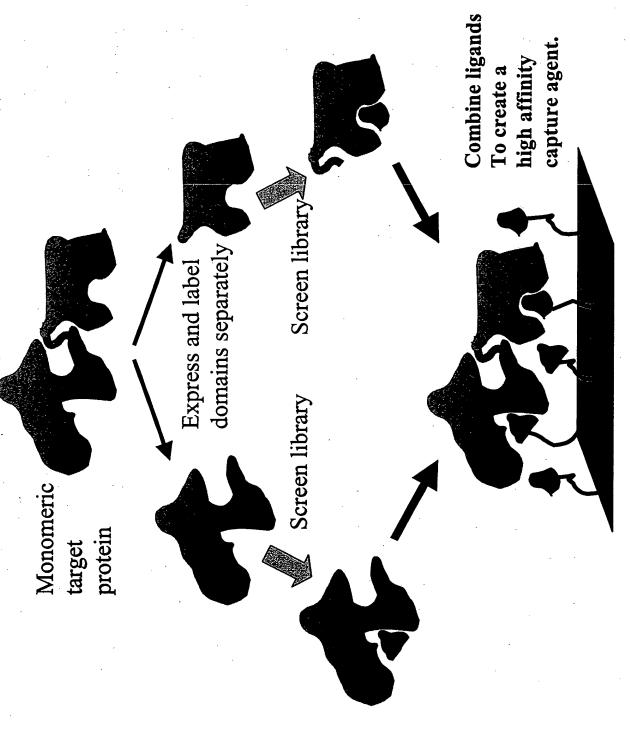


FIG. 11

13 Methoxyethylamine (Nmea)

FIG. 12

Npip-Npip-Nbsa-Nser-Nlys-Npip-Nbsa-Nlys

Nbsa-Npip-Niys-Nser-Nbsa-Nser-Nbsa-Npip

Nbsa-NIys-Npip-Nser-Nbsa-Nser-Nall-NIys <u>ල</u> <u>4</u>

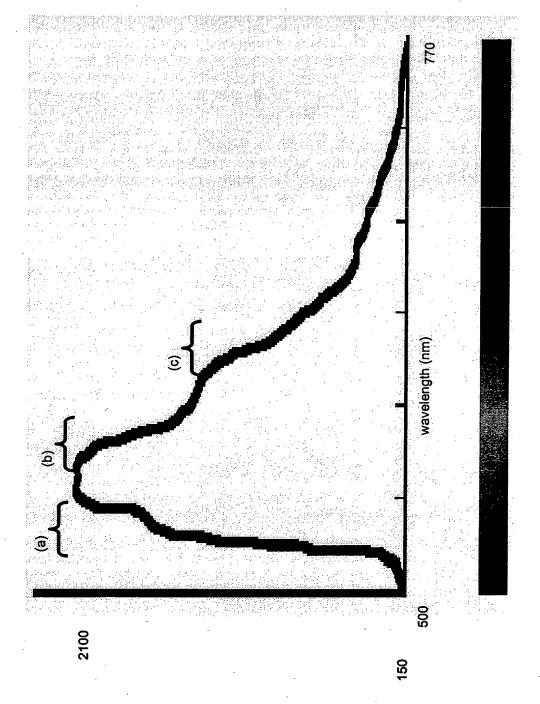
Nbsa-Nbsa-Nall-Nser-Nall-Npip-Nall-Npip

Nail-Nail-Nbsa-Nser-Niys-Nbsa-Nser-Nail 3

Niys-Niys-Nser-Nser-Npip-Nall-Nbsa-Nser 9

Niys-Niys-Nser-Nser-Npip-Nbsa-Nall-Nbsa

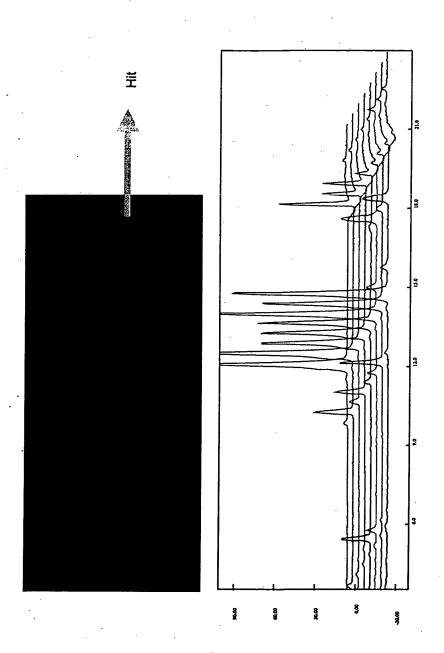
(8) Nall-Niys-Nser-Nser-Nbsa-Nser-Niys-Niys(9) Npip-Niys-Nall-Nser-Nbsa-Nser-Nbsa-Nall(10) Nbsa-Niys-Npip-Nser-Nbsa-Nser-Nall-Niys



Intensity

FIG. 14





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<u>ට</u>

€

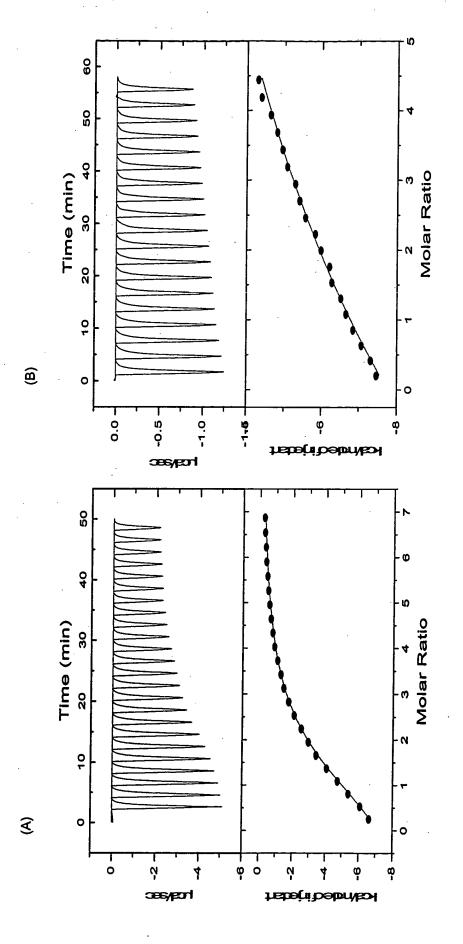
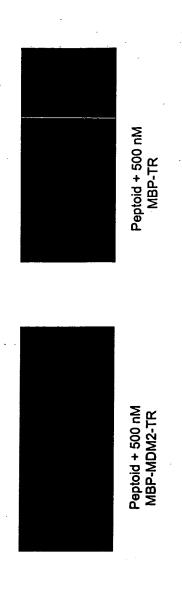


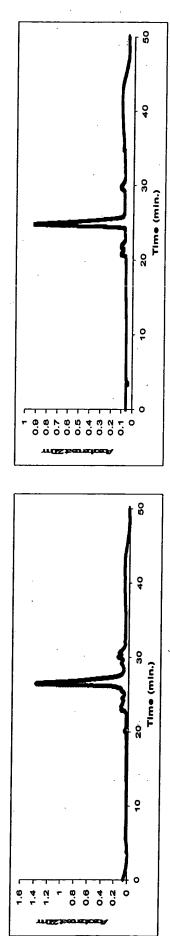
FIG. 16

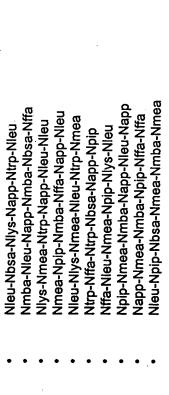


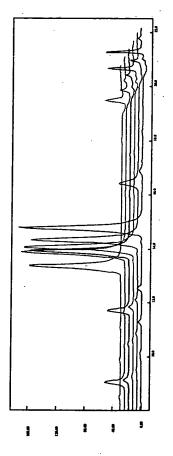


<u>B</u>

FIG. 17



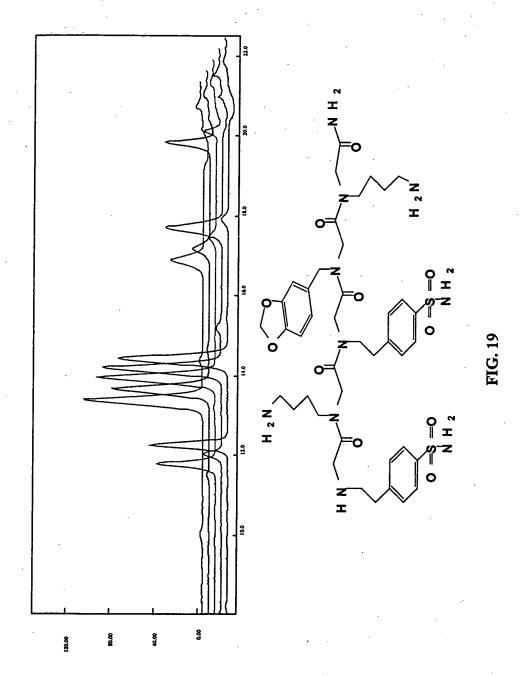




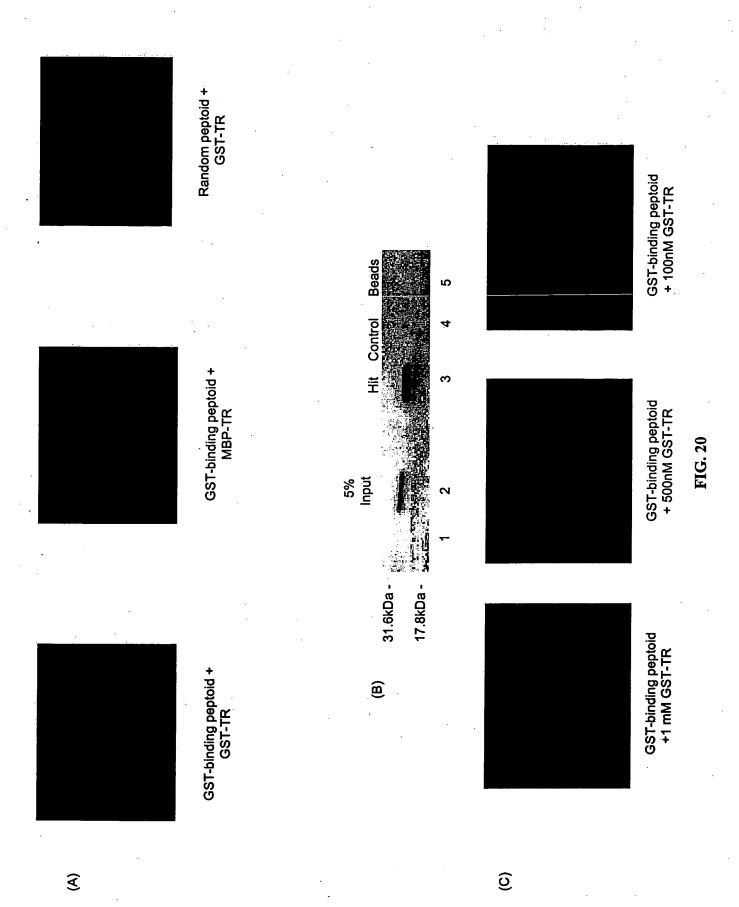
<u>@</u>

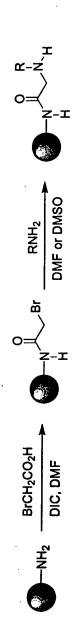
€

FIG. 18



<u>®</u>

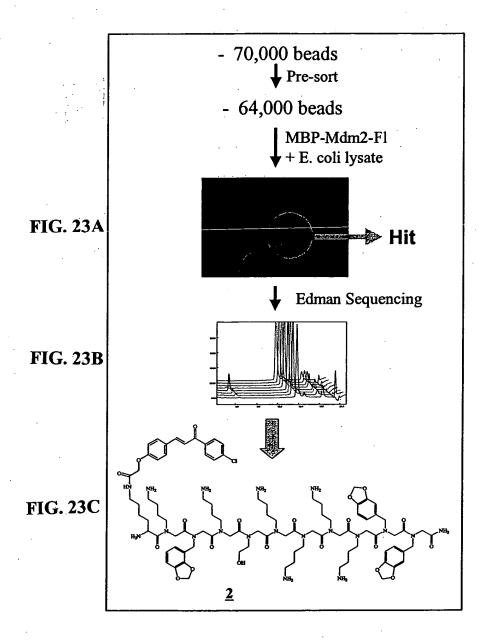




DIC: (Pr)N=C=N(Pr) R: any alkyl group

FIG. 2

FIG. 22



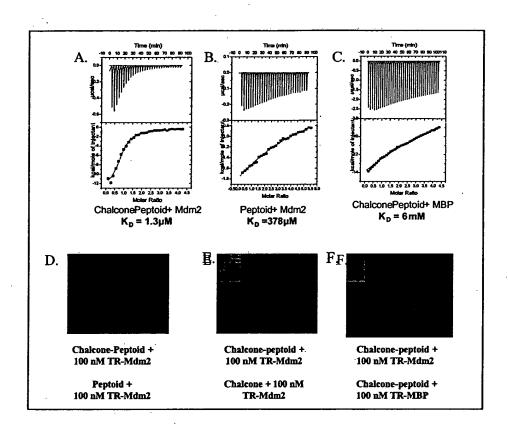


FIG. 24A-24F

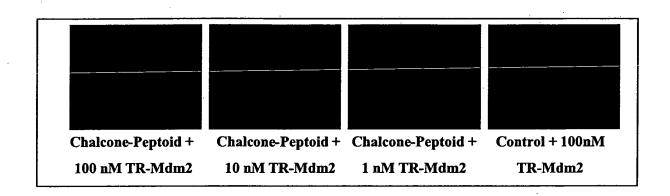


FIG 25

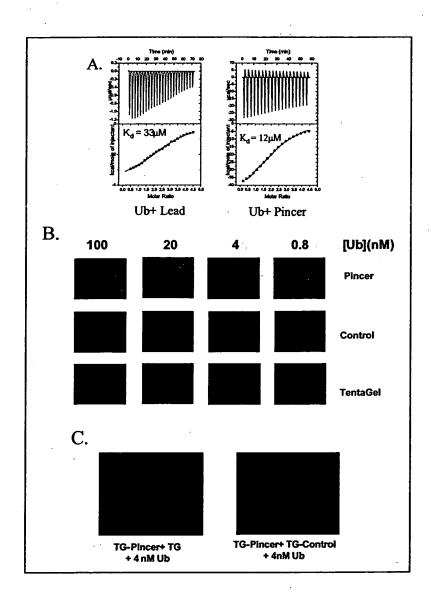


FIG. 26A-26C